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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/670,596	09/25/2003	Douglas G. Batt	PH 7440 NP	7488

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EXAMINER	
AULAKH, CHARANJIT	
ART UNIT	**PAPER NUMBER**
1625	

DATE MAILED: 05/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/670,596	BATT, DOUGLAS G.	
	Examiner	Art Unit	
	Charanjit S. Aulakh	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-22 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-22 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 3.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. According to paper filed on May 4, 2004, the applicants have elected group I with traverse for further prosecution in response to restriction requirement.

Response to Arguments

2. Applicant's arguments filed on May 4, 2004 have been fully considered but they are not persuasive regarding restriction requirement. The last office action clearly states restriction requirement and not election of species. Based on numerous variables such as R1-R25, n, u, i, z, x in the instant compounds of formula (I) covering 15 pages (183-198) for defining them, each restricted group still encompasses hundreds of thousands of species compounds and therefore, searching all groups will cause undue burdensome search.. The variables n and R3 are critical for the common core of the instant compounds, for the classification as well as for searching. Thus, restriction requirement as indicated is proper and thereby made final.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The following eight different factors (see Ex parte Foreman, 230 USPQ at 547; Wands,

In re, 858.F. 2d 731, 8 USPQ 2d 1400, Fed. Cir. 1988) must be considered in order for the specification to be enabling for what is being claimed:

Quantity of experimentation necessary, the amount of direction or guidance provided, presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability and the breadth of claims. In the instant case, the specification is not enabling based on atleast four of the above mentioned eight factors such as quantity of experimentation necessary, the amount of direction or guidance provided, presence of working examples, the state of the prior art and the breadth of claims.

The instant compounds are mentioned to modulate chemokine receptor activity (see page 1, lines 12-18). The specification also teaches that there are atleast ten different human chemokine receptors (see page 2, line 20 to page 3, line 13). However, there is no teaching in the specification regarding known utility of either agonists or antagonists at each of these ten different chemokine receptors. It is well known in the art that agonists as a particular receptor site will have opposite effect to those of the antagonists. The specification mentions some assays for determining binding affinity for CCR-2 and CCR-3 receptors or measuring intracellular calcium. However, the binding affinity demonstrated in vitro does not identify agonist versus antagonist activity of a compound in vivo. The specification does not teach which chemokine receptor is agonized or antagonized by the instant compounds. There is no teaching in the specification regarding activity of specific stereoisomers of instant compounds in any assay. Some specific stereoisomers may be inactive and therefore, won't have any

utility. There are no working examples present to show the efficacy of the instant compounds or any specific stereoisomers of these compounds in known animal models of any disease condition following their in vivo administration. The instant compounds of formula (I) encompasses hundreds of thousands of compounds based on the value of variables R1-R25, n, u, i, z, x and therefore, in absence of such teachings, guidance or presence of working examples, it would require undue experimentation to demonstrate agonist versus antagonist activity at each of the ten different known chemokine receptors and hence their utility based on prior art knowledge of role of each of these ten different chemokine receptors in specific disease conditions.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In independent claim 1, the term ---stereoisomers--- is indefinite since it is not clear which specific active stereoisomer is being reffered here. The applicants are suggested to delete this term since the utility of the instant compounds will depend upon the activity of each specific stereoisomer. Some stereoisomers may be inactive and therefore, won't have any utility.

In claim 11, the applicants are suggested to change the term ---equal—to represent.

In claim 12, the compounds of table 1 are mentioned. However, there is no table 1 in the claim. The applicants are suggested to either delete this term or include specific compounds in the claim.

In claim 14, the term----modulation of chemokine receptor activity---- is indefinite since it is not clear what is being achieved here by modulation. Which specific chemokine receptor is being reffered here and furthermore, is it being agonized or antagonized ? since the utility will be different based on agonist versus antogonist activity at specific chemokine receptor. The applicants should also include utility in the claim.

Claim 17 mentions ---compound according to claim 16 ----. However, claim 16 is a composition claim and not compound claim. Claim 17 appears substantial duplicate of claim 16 and therefore, applicants are suggested to delete this.

Claim 18 recites the limitation "method of modulating chemokine receptor activity" in claim 17. There is insufficient antecedent basis for this limitation in the claim.

In claim 19, the term ---inflammatory disorders---- is indefinite since specific disorders are not defined. The applicants are suggested to include specific disorders which are enabled by the instant specification.

Claim Rejections - 35 USC § 102

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1-9, 11, 13 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Shey (Bioorg. & Medicn. Chem. Lett., cited on applicants form 1449).

Shey discloses liquid phase combinatorial synthesis of benzylpiperazines. The compound no. 10 (see page 520) disclosed by Shey anticipates the instant claims

when both R1 and R2 represent H, Z is O and R3 represents phenyl group in the instant compounds of formula (I).

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

8. Claims 1-9, 11, 13 and 16 are rejected under 35 U.S.C. 102(e) as being anticipated by Bilodeau (WO 03/086394).

Bilodeau discloses inhiubitors of AKT activity. The compounds 1-7 and 1-8 (see table 1 on page 123) disclosed by Bilodeau anticipate the instant claims when both R1 and R2 represent H, Z is O and R3 represents phenyl group in the instant compounds of formula (I).

9. Claims 1-11 and 13-22 are objected as containing non-elected subject matter.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charanjit S. Aulakh whose telephone number is (571)272-0678. The examiner can normally be reached on Monday through Friday, 8:30 A.M. to 5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571)272-0699. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

C. S. Aulakh

Charanjit S. Aulakh
Primary Examiner
Art Unit 1625